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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,922	LISZIEWICZ ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 23-41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 23-41 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2-21-02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 2-21-02 has been entered.

Priority

This application repeats a substantial portion of prior Application No. 09/153198, filed 9-15-98, and adds and claims additional disclosure not presented in the prior application, e.g. "mixtures thereof." Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Newly submitted claims 23-41 are directed toward methods of transuding cells and methods of inducing an immune response in mammals, which is a patentably distinct invention from the products in parent application 09/153,198, now US Patent 6,240,176, filed 9-15-98.

In summary, claims 1-22 have been canceled. Claims 23-41 have been added. Claims 23-41 are under consideration.

Specification

The status of application 09/153,198 in the first line of the specification will have to be updated to reflect the fact that the application is now US Patent 6,420,176.

The status of applications throughout the specification, e.g. pg 17, line 34-38, pg 18, line 32, will require updating as necessary.

The amendment filed 2-21-02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the sentence added to the paragraph on pg 13, line 26, does not have support in the specification as originally filed. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 28-30 are objected to because they have parenthetical reference to pages of the specification. Delete references in the claim to page numbers.

Claim Rejections - 35 USC ' 112

1. Claims 23-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The genus of antigen presenting cells (APCs) in claim 23 is new matter. The specification as originally did non contemplate transducing any APCs other than dendritic cells.

The phrase "mixtures thereof" (claim 23) is considered new matter. The specification does not contemplate combining PEI with derivatives of PEI or combining different derivatives of PEI. It is noted that claim 8 as originally filed stated "wherein the complex is selected from the group consisting of DNA conjugates of sugars, polyethylenimine, polyethylenimine derivatives, and mixtures thereof"; however, the claim was rejected under indefiniteness because it could not be determined what the phrase meant (see first office action in parent application). Because of the indefiniteness of the claim as originally filed, it is not readily apparent that the phrase was intended to encompass mixing PEI with PEI derivatives or mixing different PEI derivatives as encompassed by the claims as amended. Therefore, the specification as originally filed did not support mixing PEI with PEI derivatives or different PEI derivatives.

Claim 23 is rejected under new matter because no support for the limitations in the claim has been provided. For example, "transducing APCs of the skin" in any "animal" by applying the complex to the "skin or mucosa surfaces" of the animal cannot be found in the specification as originally filed.

Claim 25 is rejected under new matter because the specification as originally filed did not complete the genus of polyethylenimine derivates that target the mannose receptor. The only such PEI described in the specification that targets the mannose receptor is mannosylated PEI as in claim 26, which is not adequate representation of the genus.

The support for a mannosylated PEI "derived from a linear PEI 22 kDA" in claim 27 cannot be found in the specification as originally filed.

Support for "electrostatically neutral" in claim 28 cannot be found on pg 25, lines 26-27 or pg 24.

The phrase "about 3-10:1 molar equivalents" (claim 29) or "about 5:1 molar equivalents" (claim 30) is new matter. Support for the limitations of claims 29 and 30 cannot be found on pg 25, lines 26-27 and pg 24. Page 22, lines 9-16, teaches that at the 5:1 (N:P) ratio, PEI-man-DNA is neutral. The specification states that N and P stand for nitrogen and phosphorus; however, the specification does not state that the N must be from polyethylenimine and the P must be from the DNA as claimed. Nor does the specification distinguish that molar equivalents and not the number of nitrogen and phosphorus determine the 5:1 ratio. Nor does the specification contemplate the molar ratio is "about 5". Therefore, the phrases are new matter.

The phrase "glucose solution" in claim 31 is found on pg 22, lines 35-36.

The phrase "about 5-10" (claim 32) and "about 8" (claim 33) are new matter. The specification on page 22, lines 33-36, state that DNA was mixed in 100 mM PEI-man in a 5-10% glucose solution (optimum 8%). The specification does not contemplate expanding the range of 5-10% or 8% to about 5-10% or 8%. Therefore, use of "about" with 5-10% or 8% was not contemplated in the specification as originally filed.

Support for the limitation of activating the APCs of the skin or mucosa in claim 34 cannot be found and is new matter.

Support for the limitation of activating the APCs of the skin or mucosa by receptor stimulation, toxin activation, or tissue or cell injury in claim 35 cannot be found and is new matter.

Support for proteins "derived" from a reverse-transcriptase dependent virus in claim 36 cannot be found and is new matter. The term "derived" is not in the specification as originally filed in context of proteins isolated from viruses. The genus of RT-dependent viruses was not contemplated in the specification as originally filed. The species of HIV as in claim 37 does not represent the genus.

2. Claims 23-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for reasons of record.

The claims are drawn to transducing antigen presenting cells (APCs) of the skin by applying a complex to the skin or mucosa of an animal, wherein the complex comprises i) DNA encoding a an immunogenic protein and ii) sugar, polyethylenimine (PEI), a PEI derivative, or mixture thereof.

The specification suggests using the method claimed to induce an immune response in a mammal (pg 20, Example 4). However, merely inducing an immune response in a mammal, in and of itself, does not have a use by itself because inducing an immune response is only described in the specification as being used to obtain a therapeutic or prophylactic effect (pg 2, lines 20-24; pg 18, lines 2-8). Therefore, inducing an immune response according to the specification must result in a therapeutic or prophylactic effect to have an enabled use. The methods using DNA encoding an immunogenic protein as claimed lack written description because the specification does not provide adequately describe how to induce a therapeutic or prophylactic immune response using the method claimed.

The genus of antigen presenting cells (APCs) in claim 23 lacks written description. The specification as originally did non contemplate transducing any APCs other than dendritic cells. The species of dendritic cells is not adequate to support the genus of APCs.

Claims 36-39 require using DNA encoding a protein derived from a reverse-transcriptase dependent virus. Applicants describe using plasmids encoding

replication-defective, integrase-defective retroviruses in the method claimed which are described in related application 08/989,301 as non-lethal and capable of inducing a therapeutic/prophylactic immune response. However, Adachi (J. Virol., Aug. 1986, Vol. 59, pg 284-291) taught such viruses were still infectious. "Replication defective retroviruses" that are non-lethal and capable of inducing a therapeutic/prophylactic immune response are not adequately described by applicants. Nowhere have applicants provided any evidence that the amount of expression of viral protein is adequate to induce a therapeutic/prophylactic immune response or that the virus does not replicate too much and cause disease. Use of the plasmids encoding replication-defective retrovirus in animals as claimed would not treat or prevent disease because the virus would replicate and cause disease. Applicants appear to be attempting to find a retrovirus that expresses adequate viral antigen such that a cellular immune response can be obtained, wherein said retrovirus replicates to a low degree without causing disease. Naming a type of material that may exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming a method of using replication-defective retroviruses without defining what means will induce a therapeutic/prophylactic effect without causing infection is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

The phrase "PEI, PEI derivatives and mixtures thereof" in claim 23 lacks written description. The specification does not contemplate combining PEI with derivatives of PEI or combining different derivatives of PEI. It is not readily apparent that applicants were in possession or even contemplated any "mixture thereof" as broadly claimed.

3. Claims 23-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

The claims are drawn to transducing antigen presenting cells (APCs) of the skin by applying a complex to the skin or mucosa of an animal, wherein the complex comprises i) DNA encoding a an immunogenic protein and ii) sugar, polyethylenimine (PEI), a PEI derivative, or mixture thereof.

The specification describes using the method claimed to induce an immune response in a mammal (pg 20, Example 4). However, merely inducing an immune response in a mammal, in and of itself, does not have an enabled use by law because inducing an immune response is only described in the specification as being used to obtain a therapeutic or prophylactic effect (pg 2, lines 20-24; pg 18, lines 2-8). Therefore, inducing an immune response according to the specification must result in a therapeutic or prophylactic effect to have an enabled use. The ordinary artisan reading

the claimed invention in view of the specification would only determine that the method claimed was for the purpose of therapy or prophylaxis. Applying DNA encoding an immunogenic protein to an animal as claimed is not enabled because the specification does not provide adeqaute guidance for one of skill to induce a therapeutic or prophylactic immune response using the method claimed.

Klatzmann and Sticker taught retroviral vaccines have been unable to protect against infection (Klatzmann, US Patent 6,140,114, Oct. 31, 2000; Stricker et al., Medical Hypotheses, June 1997, Vol. 48, pg 527-9). Overall, a lack of understanding about protective immunity to retroviruses such as HIV, the sequence variability and the rapid replication of retroviruses contribute the ineffectiveness of vaccines against retroviruses (Bangham, Nov. 29, 1997, Lancet, Vol. 350, pg 1617-1621; pg 1617, top of col. 1).

The specification teaches making plasmids encoding replication defective, integrase-defective HIV as described in application 08/989,301 (pg 18, line 30-32). In application 08/939,301, applicants call such retroviruses "Class 4" viruses which are infectious but replication-defective (pg 15, lines 1-5). In application 08/989301, applicants teach that replication defective HIV that does not replicate effectively is inadequate to elicit a protective cellular immune response. Alternatively, replication defective HIV that does replicate effectively causes disease and sometimes fatal (pg 3, line 17 through pg 4, line 3). The amount of replication of a retrovirus required to obtain

a therapeutic cellular immune response without causing disease was unknown in the art at the time of filing. It was also unknown how to make a retrovirus with the adequate amount of replication that would provide an adequate cellular immune response without causing disease. Without being able to make such a retrovirus, it was unknown how to use such a virus to obtain a therapeutic or prophylactic cellular immune response in a host.

The specification does not provide adequate guidance regarding how to obtain a therapeutic or prophylactic effect by applying a replication defective retrovirus in an animal as claimed. The specification does not teach the amount of a cellular immune response that is therapeutic or prophylactic effect against a replication defective retrovirus. The amount of dendritic cells required to obtain adequate antigen presentation is not provided in the specification. The amount of retroviral protein expression required to obtain the desired cellular immune response is not provided in the specification. The amount of replication and infectiousness required to obtain the desired balance between therapy and pathogenicity is not provided in the specification. Given the teachings in the specification taken with the unpredictability in the art at the time of filing, it would have required one of skill in the art at the time of filing undue experimentation to determine how to make and/or use a replication defective retrovirus to obtain a therapeutic/prophylactic effect without causing disease or death.

In addition, it was unpredictable what vector, promoter, dosage, cells, level of expression and route of administration would provide a therapeutic or prophylactic effect using *in vivo* or *ex vivo* gene therapy (Miller 1995, FASEB J., Vol. 9, pg 190-199; pg 198, col. 1; Deonarain, 1998, Expert Opin. Ther. Pat., Vol. 8, pg 53-69; pg 53, 1st ¶, pg 65, 1st ¶ under Conclusion section; Verma, Sept. 1997, Nature, Vol. 389, pg 239-242; see entire article, specifically pg 240, sentence bridging col. 2 and 3; Crystal, 1995, Science, Vol. 270, pg 404-410, pg 409; Ross, Sept. 1996, Human Gene Therapy, Vol. 7, pg 1781-1790; pg 1782, col. 2, 1st full ¶; pg 1789, col. 1, 1st ¶).

The specification does not enable applying DNA to the mucosa to target APCs of the skin. It is unclear how application of DNA to the mucosa would result in expression of the protein in the skin. The specification does not provide the combination of vector, promoter, dosage, level of expression that would result in a therapeutic/prophylactic effect. Given the teachings in the specification taken with the unpredictability in the art at the time of filing, it would have required one of skill in the art at the time of filing undue experimentation to determine the vector, promoter, cell, dosage, level of expression and route of administration required to obtain a therapeutic or prophylactic effect using the method claimed.

3. Claims 23-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is indefinite because it is unclear whether "mixtures thereof" refers to mixtures of sugars, PEI and PEI derivatives or to mixtures of DNA with sugars, PEI or PEI derivatives.

Claim 23 is indefinite because the preamble requires transducing APCs of the skin, but the body of the claim merely requires applying a complex to the skin/mucosa of an animal. It is unclear if transduction of APCs and expression of the immunogenic protein are clear, positive steps that must occur in the body of the method claimed.

Claim 23 is indefinite because the complex may be applied to the mucosa surface of an animal but the preamble requires transduction of APCs of the skin. It is unclear how APCs of the skin can be transduced by application of the complex to the mucosa.

Claim 23 is indefinite because it is unclear if "transduction" is limited to infection with a virus or if it encompasses transfection with plasmid. The specification does not define "transduction"; however, the art sometimes refers to "transduction" as infection with a viral particle. In view of claim 40, which is limited to plasmid, use of the term "transduction" is confusing.

Claim 23 is indefinite because the metes and bounds of what applicants consider "applying" to the skin cannot be determined. It is unclear if the phrase is limited to putting the complex on the skin or if the phrase encompasses subcutaneous injection which results in delivery of the complex under the skin. It is unclear if intravenous injection is encompassed by the phrase because such an injection does require contact of the complex to the skin when the injection passes through the skin.

Claim 27 is indefinite because it is unclear what applicants consider a mannosylated PEI "derived" from a line PEI 22kDA. The metes and bounds of "linear" PEI cannot be determined. The phrase "a linear PEI 22kDA" is confusing because it is unclear if the line PEI is 22kDA in weight or if PEI 22 kDA refers to some particular type of PEI.

Claim 29 and 30 are indefinite because the phrases "about 3-10:1 molar equivalent polyethylenimine or polyethylenimine derivate amine per DNA phosphate ratio" and "about 5:1 molar equivalent polyethylene mine or polyethylene mine derivate amine per DNA phosphate ratio" are unclear. Page 22, lines 9-16, teaches that at the 5:1 (N:P) ratio, PEI-man-DNA is neutral. The specification states that N and P stand for nitrogen and phosphorus. It is unclear if the phrase is intended to be the limited to the ratio of polyethylene mine derivate amine per DNA phosphate or encompasses the ratio of polyethylene mine derivate amine or polyethylene mine amine per DNA phosphate. The phrase "molar equivalent polyethylenimine" seems to be missing a word making the

phrase unclear. The metes and bounds of the phrase also cannot be determined because it is unclear what applicants consider "about 5 molar equivalents" of N and P.

Claim 31 is indefinite because it is unclear whether a "glucose solution" encompasses glycosylated PEI (a derivative of PEI as in claim 23) or is limited to glucose in water. The specification teaches PEI may be glycosylated (pg 21, Table 1) or solubilized in glucose (pg 22, line 35). Overall, it is unclear whether the glucose solution is a solution in which the complex of claim 23 is put in or encompasses a complex made up of PEI conjugated with glucose.

Claims 32 and 33 are indefinite because the metes and bounds of the phrase "about 5-10% glucose" and "about 8% glucose" cannot be determined. The specification does not teach how to determine the units of the 5-10% glucose described on page 22, line 35-36. Thus, the metes and bounds of the claims cannot be determined.

The phrase "activating the antigen presenting cells" in claim 34 is indefinite. It is unclear if the phrase is further limiting what happens when the complex is "applied" as in claim 23 or if it is a step that is separate from "applying" the complex that occurs before or after "applying" the complex. It is unclear if "activation" refers to expression of the immunogenic protein in the context of an MHC molecule or to a second, separate step that causes "activation" of the APCs, e.g. applying an interleukin that causes APC activation.

The metes and bounds of what applicants consider "activating" APCs by receptor stimulation, toxin activation, or tissue or cell injury in claim 35 cannot be determined. It is unclear if applicants are attempting to limit how the complex enters the APCs after being applied or if receptor stimulation, toxin activation, or tissue or cell injury causes the APCs to express the immunogenic protein in a particular manner.

The metes and bounds of proteins "derived" from a reverse transcriptase dependent virus are unclear. It is unclear if the proteins must be isolated from such a virus or must be altered from their natural state (i.e. derived). Deletion of the term "derived" is recommended.

The metes and bounds of what applicants consider a reverse transcriptase dependent virus in claims 36 and 27 is unclear. It is unclear if the claim is limited to lentiviruses or if the claim encompasses other viruses that are somehow dependent on reverse transcriptase. If the phrase is intended to encompass non-lentiviruses, it cannot be determined how such viruses might be dependent upon reverse transcriptase.

Claim Rejections - 35 USC ' 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 23-35, 40 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by Behr (US Patent 6,013,240, Jan. 11, 2000; 102(e) date=2-28-97)

The parent application 60/058,933, does not describe complexing DNA with a compound selected from the group consisting of sugars, PEI, PEI derivatives, or mixtures thereof (claim 23). Therefore, the claimed invention does not get priorty back to 9-15-97. Parent application 09/153,198 does not describe complexing DNA with a glucose solution (claim 31). Therefore, the claims in general have priority to 9-15-98, except for claims 31-33 relating to a "glucose solution," which have an effective filing date of 2-21-02.

Behr taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter suspended in 5% glucose (col. 12, lines 53-57). Luciferase is an immunogenic protein because it is foreign to mammals and induces an immune response in mammals. Behr taught administering the complex to the skin or mucosa of an animal (claim 33, col. 6, lines 1-19).

Claims 25-27 are included because they are not limited to a compound that is mannosylated PEI or PEI "derived from a linear PEI 22 kDA;" claims 25-27 encompass glucose as in parent claim 24.

Claims 28-30 are included because Behr taught that between 5-20 equivalents of PEI amines are used relative to DNA phosphates (col. 8, lines 15-19), specifically 9 equivalents (col. 12, line 58). The instant specification teaches that such ratios cause the complex to be electrostatically neutral (¶ bridging pg 21-22).

Claim 33 is included because 5% is "about 8%" as claimed.

Claims 34, 35 and 41 are included because administering the complex to the skin/mucosa as taught by Behr inherently would activate APCs by toxin activation. Cells would start expressing luciferase and this firefly "toxin" would be recognized as foreign by the animal, thereby activating APCs, including Langerhans cells.

Claim Rejections - 35 USC ' 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 23-38, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (US Patent 6,013,240, Jan. 11, 2000) in view of Adachi (J. Virol., 1986, Vol. 59, pages 284-291) and Owada (Microbiol. Immunol. Feb. 1998, Vol. 242, No. 2, pg 97-107).

The parent application does not describe a "glucose solution" (claim 31). Therefore, the effective filing date of claims 31-33 is the filing date of parent application 09/153,198, which is 9-15-98.

Behr taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter suspended in 5% glucose (col. 12, lines 53-57). Luciferase is an immunogenic protein because it is foreign to mammals and induces an immune response in mammals. Behr taught administering the complex to the skin or mucosa of an animal (claim 33, col. 6, lines 1-19). Behr did not teach the immunogenic protein was derived from a reverse transcriptase dependent virus.

However, Adachi taught a plasmid encoding replication-defective HIV used for transfecting a wide array of eukaryotic cells (pg 284, col. 2, 8 lines from the bottom; pg 285, col. 1, Table 1; pg 289, Table 2).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to administer a complex of a plasmid encoding an immunogenic protein and PEI in a glucose solution to the skin/mucosa of an animal to express the protein in cells of the animal as taught by Behr wherein the plasmid encoded HIV proteins as taught by Adachi. One of ordinary skill in the art would have been motivated to use PEI to administer the plasmid of Adachi because PEI increased transfection as compared to DNA alone (Behr, col. 8, lines 13-19; col. 13, lines 6-10). One of ordinary skill in the art would have been motivated to replace the plasmid encoding luciferase with the plasmid encoding HIV proteins to determine whether an immune response against the HIV antigens would occur *in vivo*. One of ordinary skill in the art at the time the invention was made would have been motivated to use PEI to deliver DNA encoding HIV proteins because it was well known in the art at the time of filing that PEI could be used to deliver DNA encoding HIV proteins to cells (Owada, see pg 98, "Cells and Virus", "Compounds").

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

6. Claims 23-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behr (US Patent 6,013,240, Jan. 11, 2000) in view of Adachi (J. Virol., 1986, Vol. 59, pages 284-291) and Owada (Microbiol. Immunol. Feb. 1998, Vol. 242, No. 2, pg 97-107) as applied to claims 23-38, 40 and 41, further in view of Holler (US Patent 5,908,923).

The parent application does not describe a "glucose solution" (claim 31). Therefore, the effective filing date of claims 31-33 is the filing date of parent application 09/153,198, which is 9-15-98.

The combined teachings of Behr, Adachi and Owada taught a complex comprising i) PEI, and ii) plasmid DNA comprising a nucleic acid sequence encoding an HIV protein operatively linked to a promoter suspended in 5% glucose (see 103 rejection above). The combined teachings of Behr, Adachi and Owada did not teach the immunogenic protein was derived from an integrase defective HIV virus.

However, Holler taught a plasmid encoding replication-defective HIV that was integrase defective for use in vivo (col. 4, lines 51-54).

Thus, it would have been obvious for one of ordinary skill in the art at the time the invention was made to administer a complex of a plasmid encoding an HIV protein and PEI in a glucose solution to the skin/mucosa of an animal to express the protein in cells of the animal as taught by the combined teachings of Behr, Adachi and Owada wherein the plasmid encoding HIV proteins was integrase defective as taught by Holler. One of

ordinary skill in the art would have been motivated to make the HIV integrase defective to prevent causing disease in the animal.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

Claims 23-41 of this application conflict with the claims of Application No. 08/989,301. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Claims 23-41 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 08/989,301. Although the conflicting claims are not identical, they are not patentably distinct from each other because they require administering DNA encoding retroviral proteins to the skin/mucosa/dendritic cells of an animal.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following prior art is being made of record and not relied upon because it is considered pertinent to applicant's disclosure:

The proceedings of the 3rd European conference on gene therapy of cancer, held from Sept. 11-13, 1997 at the University of Berlin, as supported by Diebold (Diebold et al., Advances in Experimental Med. and Biol., Oct. 1998, Vol. 451, pages 449-455). The preface of Advances in Experimental Med. and Biol., Oct. 1998, Vol. 451 (page v and vi) states that Vol. 451 contains the proceedings of the 3rd European conference on gene therapy of cancer. At the conference Diebold taught a complex comprising i) mannosylated PEI (PEI-man), and ii) plasmid DNA comprising a nucleic acid sequence encoding luciferase operatively linked to a promoter used to transfect dendritic cells via the mannose receptor (pg 452, line 10; pg 453, line 13-18). While Diebold described using a complex comprising PEI-man and DNA encoding an immunogenic protein at least a year and two days prior to the filing date of the instant application (Sept. 15, 1998), the conference was in Germany. 102(a) and (b) requires that the information known in this country or published in this country or a foreign country prior. It does not appear that the information disclosed by Diebold was known in this country or published in any country until the publication of Advances in Experimental Med. and Biol., Vol. 451 in Oct. 1998. Therefore, the information disclosed by Diebold at the conference is not available under 102(a) or (b).

US Patent 6,420,176, application 09/153,198, claims a composition comprising DNA and mannosylated polyethylenimine, wherein said DNA encodes at least one immunogenic protein. The composition claims were restricted from the methods of using the composition in application 09/153,198.

Song (PNAS, March 1997, Vol. 94, pg 1943-1948) taught administering retroviral particles encoding HIV IIIB env/rev to mice intramuscularly (pg 1943, col. 2, "Retroviral vectors" and "Immunizations...") or with dendritic cells transduced with the virus injected intraperitoneally (pg 1943, col. 2, "Retroviral vectors" and "Immunizations...").

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER